

## Symptoms of overactive bladder (OAB) in patients treated for depressive disorders

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### Summary

**Aim:** The aim of the study was to investigate the correlation between symptoms of overactive bladder (OAB) and severity of depressive symptoms in patients treated for depression.

**Method:** 102 patients (43 males, 59 females) aged 20–67 ( $M = 46.1 \pm 11.3$ ) treated for depression were included in this cross-sectional analysis. OAB symptoms were examined with the International Prostate Symptom Score (IPSS) and International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB). OAB-related quality of life was assessed with the International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module (ICIQ-OABqol). Depressive symptoms were assessed with the 17-item Hamilton Depression Rating Scale (HDRS) and Quick Inventory of Depressive Symptomatology – Self Report (QIDS-SR).

**Results:** Symptoms of OAB assessed with IPSS and ICIQ-OAB were more severe in women than in men. In the entire group highest scores in IPSS of assessed OAB symptoms were observed in nocturia ( $1.53 \pm 1.64$ ) followed by urinary frequency ( $1.19 \pm 1.48$ ) and lowest in urgency ( $0.80 \pm 1.28$ ). Symptoms of OAB (based on the ICIQ-OABqol total score) were more bothersome in women ( $48.74 \pm 29.18$ ), than in men ( $39.18 \pm 17.70$ ). In the whole group and in women the QIDS-SR total score correlated with the ICIQ-OAB score ( $p < 0.05$ ). The total QIDS-SR score correlated with the ICIQ-OABqol score in entire group ( $p < 0.05$ ), in women ( $p < 0.05$ ) and in men ( $p < 0.05$ ). Patients suffering from at least moderate depression assessed with QIDS-SR had significantly more pronounced symptoms of urinary frequency ( $p = 0.005$ ) and urgency ( $p = 0.039$ ). A number of other significant ( $p < 0.05$ ) correlations were observed between the total ICIQ-OAB score and certain items' scores in the GHQ-30 both in women.

**Conclusions:** OAB symptoms are common among patients treated for depressive disorders. There is a correlation between severity of depressive symptoms and OAB. OAB is bothersome and affects the quality of life in patients treated for depression. Comorbidity of OAB and depression has clinical significance and that should enhance interdisciplinary treatment approaches. Due to limitations of this study, further researches are essential to reveal more details of the correlation between OAB and depression.

depression, OAB, LUTS, comorbidity

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### INTRODUCTION

Overactive Bladder (OAB) refers to, according to International Continence Society (ICS) defini-

tion from 2002, the occurrence of urinary urgency usually accompanied by pollakiuria (urination 8 or more times a day, or according to recent diagnostic trends such frequency, which is associated with annoyance and a decrease in quality of life) and nokturia (the complaint that the individual has to wake at night one or more times for voiding and urinating is preceded by a period of sleep, which also follows), with a possible urine incontinence [1].

The above symptoms belong to the lower urinary tract symptoms (LUTS), and more specifically to the LUTS related to urinary accumulation [1]. The diagnosis of OAB, based on collecting the accurate patient's medical record and physical examination, requires exclusion of urinary tract infection and other urinary tract pathologies. It is a common health problem. In multicentre studies carried out up to now, on large groups representative of the general population, the incidence of OAB was 9-43% in the examined women and 7-27% in men [2-6]. The incidence of OAB symptoms increases with age, both in women and in men [5-6].

In most cases, it is a chronic condition, and in some patients the symptoms persist until the end of life, despite treatment [7-9]. Treatment is currently based mainly on behavioral techniques, lifestyle changes and pharmacotherapy, and in case of the absence of their effectiveness, invasive methods are also used [9]. The authors of the cited Canadian guidelines for the management of OAB in adults [9] to behavioral techniques include bladder training (BT) and pelvic floor muscle therapy (PFMT). Lifestyle changes that may have a positive effect on the course of OAB include, inter alia, control of the amount of consumed fluids and caffeine, change of diet and weight loss in the case of obese patients, proper treatment of other co-occurring somatic diseases, cessation of smoking, as well as the introduction of regular physical effort.

OAB pharmacotherapy is based mainly on antimuscarinic drugs (e.g. oxybutynin, tolterodine, darifenacin, fesoterodine, solifenacin) and beta-3 adrenergic receptor agonists (mirabegron). The invasive methods of OAB treatment include botulinum toxin type A injections into the detrusor muscle and sacral neuromodulation (SNM). Some patients also use peripheral tibial nerve stimulation (PTNS). The long-term occurrence

of OAB symptoms is associated with a significant decrease in quality of life, deterioration of physical, sexual, social and sleep quality [10-12].

The work published so far on the general population indicate the existence of a positive correlation between OAB and depression. In a cross-sectional, multicenter EpiLUTS study conducted on a representative group of both women and men with annoying OAB symptoms reported higher levels of anxiety and depression compared to patients with or without OAB symptoms [13-15]. A clinical-control analysis based on the results of another large Epidemiology Urinary Incontinence and Comorbidities (EPIC) study showed a statistically more frequent occurrence of depression in OAB subjects than in the control group (148 and 46, respectively,  $p < 0.001$ ) [10]. Also, the National Overactive Bladder Evaluation (NOBLE) program in the United States carried out to assess the prevalence and significance of OAB, confirmed a statistically significant higher incidence of depression in subjects with OAB compared to healthy subjects [5,16]. The relationship between depression and OAB is bidirectional. The above results indicate the coexistence of OAB with depression, while other studies have observed new cases of OAB in depressed patients [17-21], and some researchers describe new cases of depression in patients with OAB [18-19].

Authors of a review paper, describing inter alia the studied so far relationship between depression and anxiety with OAB, presented, according to the current state of knowledge, possible explanation of pathomechanisms combining OAB with depression [22]. They paid special attention to the low level of health-related quality of life, sleep disorders and reduced self-esteem of patients with OAB, stress associated with the occurrence of depression, as well as with joint depression and OAB biological factors associated with serotonergic and adrenergic activity, disturbed by regulation hypothalamic-pituitary-adrenal pituitary axis, changes in the limbic system and perfusion disorders of the cerebral cortex. The use of urological and psychiatric drugs also modulates the course of both depressive symptoms and OAB. However, the exact nature of these dependencies is still largely unknown.

The following study is the first in Poland work on the relationship between OAB and depres-

sion in patients suffering from it. Recently, the first Polish work investigating the occurrence of LUTS in patients treated for depression [23] was published. In this study, a statistically significant relationship between depression and LUTS was observed. It also confirmed the high frequency and significant severity of LUTS symptoms in this group of patients. The severity of depressive symptoms correlated positively with the severity of LUTS symptoms examined using the QIDS-SR Inventory (Quick Inventory of Depressive Symptomatology – Self Report) and the International Prostate Symptom Score (IPSS) respectively. The strong negative impact of the experienced symptoms of depression and LUTS on the quality of life of patients was also confirmed. These are observations of high clinical significance. This work is a continuation and development of these studies on OAB issues.

## AIM

The aim of the study was to assess the severity of OAB symptoms depending on the severity of psychopathological symptoms in patients treated for depressive disorders.

## METHODS

### Subjects

The cross-sectional study included patients who were 18 years or older and were treated in an outpatient base in mental health clinic or in psychiatric departments because of depressive disorders. The study was approved by the Bioethical Committee of the Jagiellonian University (no. KBET / 266 / B / 2013). Each participant gave informed consent for participation in the study. All subjects completed the patient's clinical observation chart.

### DIAGNOSTIC TOOLS

The International Prostate Symptom Score (IPSS), the International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB) and the International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module (ICIQ-OABqol)

were used to assess the severity of OAB symptoms. The IPSS scale was created in 1992 by the American Society of Urology [24]. It was used repeatedly to assess the severity of LUTS in both men and women [23, 25-28]. The scale contains 7 questions about LUTS (four concern the symptoms of the collection phase, three – the emptying phase) and one is related to the quality of life. For questions about urological symptoms, the examined respond on a scale 0 to 5, indicating the severity of symptoms, and the overall score may be from 0 to 35 points (no symptoms to very severe symptoms). The question about the quality of life associated with LUTS is rated on a scale of 0 to 6 (excellent – unbearable). ICIQ-OAB and ICIQ-OABqol questionnaires were developed in the company of International Consultation on Incontinence (ICI) and are used to assess the severity of symptoms of bladder hyperactivity [29-30] and the specific OAB-related quality of life [31]. These are specialized, validated and ones of the most frequently used questionnaires on OAB issues. The ICIQ-OAB questionnaire consists of 8 questions regarding the severity of the frequency of pollakiuria, nocturia, urgency and urinary incontinence, and the degree of annoyance for each of the symptoms on a scale. The ICIQ-OABqol questionnaire consists of 25 questions assessing the impact of bladder related symptoms on quality of life. Questions relate to limitations of the possibility of traveling, feelings of worry, frustration, sleep disorders, nocturia, avoiding social events, worsening relationships with the loved ones.

The presence and severity of depressive symptoms were examined using the Hamilton Depression Rating Scale (HDRS) and the Quick Inventory of Depressive Symptomatology – Self Report (QIDS-SR). HDRS has been used for many years to study the severity of depressive symptoms [32-33], also in patients with LUTS [23, 34-35]. The QIDS-SR self-assessment scale is also widely used to assess the severity of depression, has good psychometric properties, is equally sensitive and its results correlate with the results of the 30-item Inventory of Depressive Symptomatology (IDS) and the 24-item Hamilton Rating Scale for Depression [36-37] and was recently used in the first Polish work examining the relationship between depression and LUTS [23]. The ranges of the scores in

QIDS-SR are defined as follows: remission (0-5 points), mild depression (6-10 points), moderate depression (11-15 points), severe depression (16-20 points), very severe depression (21-27 points) [36]. The General Health Questionnaire (GHQ-30, a Polish translation by Małyszczak et al.) is used for screening the mental health status of adults in the general population [38-40].

STATISTICAL METHODS

In the description of the studied group, the arithmetic mean and standard deviation were used (SD). Pearson’s correlation was applied as-

sess the relations. Chi2 NW tests and Student’s t tests for two independent samples were also performed. The deviation was normal (Shapiro-Wilk test). P scores below than or equal to 0.05 were considered statistically significant. Statistical analysis was performed using the STATISTICA 12 program (UJ CM license)

RESULTS

102 people were examined: 43 men (42.16%) and 59 women (57.84%). The characteristics of the group are shown in Table 1.

Table 1. Characteristics of the studied group

Number of respondents	n = 102 (100%)
The average age of the respondents	46.1±11.3 lat
The average BMI value	26.72±5.19 kg/m2
The average duration of previous psychiatric treatment	10.7±8.6 lat
The average number of hospitalizations	2.4±3.5
Sex	
Men	n = 43 (42.16%)
Women	n = 59 (57.84%)
Marital status	
Married	n = 68 (66.66%)
Divorced	n = 9 (8.82%)
In separation	n = 3 (2.94%)
Informal relationships	n = 5 (4.9%)
Single	n = 17 (16.66%)
Education	
Primary	n = 3 (2.94%)
Secondary	n = 35 (34.31%)
Professional	n = 11 (10.78%)
Higher	n = 53 (51.96%)
Professional status	
Employed	n = 54 (52.94%)
Pension	n = 28 (27.45%)
Unemployment	n = 12 (11.76%)
Education	n = 5 (4.9%)
Retired	n = 3 (2.94%)
Place of residence	
Village	n = 32 (31.37%)

City	n = 70 (68.63%)
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Table 2. Results in HDRS and QIDS-SR scales

	Females (N=59 )	Males (N=43 )	All (N=102 )
HDRS (M, SD)	15.33±9.50	15.44±8.27	15.38±8.96
QIDS-SR (M, SD)	14.44±6.16	13.8±6.71	14.17±6.37

The results obtained in the HDRS and QIDS-SR scales are presented in Table 2.

Evaluation of the severity of symptoms based on the results of HDRS and QIDS-SR questionnaires is presented in Table 3.

Table 3. Degree of severity of depressive symptoms in HDRS and QIDS-SR

Severity	HDRS (N. %)	QIDS-SR (N. %)
Remission	20 subjects (19.6%)	12 subjects (11.76%)
Mild	24 (23.52%)	18 (17.64%)
Moderate	27 (26.47%)	31 (30.39%)
Heavy	18 (17.64%)	20 (19.6%)
Very heavy	13 (12.74%)	20 (19.6%)

In the next step, IPSS scores were calculated (Table 4). The average point value among all respondents in the IPSS scale was  $8.07 \pm 8.76$ . The highest average point value (highest severity of complaints) among all subjects from all IABS-assessed OAB symptoms achieved: nocturia ( $1.53 \pm 1.64$ ) and pollakiuria ( $1.19 \pm 1.48$ ), and the lowest – the urge pressure ( $0.80 \pm 1.28$ ). In the studied group of men, the highest mean point value (the highest severity of complaints) among those assessed by the IPSS scale of OAB symptoms achieved: nocturia ( $1.25 \pm 1.54$ ) and pollakiuria ( $0.81 \pm 1.20$ ), and the lowest urge pressure ( $0.39 \pm 1.04$ ). Similarly, in the group of

women surveyed, the highest mean point value among the OAB symptoms assessed on the IPSS scale achieved: nocturia ( $1.74 \pm 1.69$ ) and pollakiuria ( $1.47 \pm 1.62$ ), and the lowest – urge pressure ( $1.10 \pm 1.61$ ).

The results of the Chi2 NW test indicated relationships between the severity of each of the OAB symptoms assessed and the severity of depressive symptoms in the QIDS-SR scale (remission or mild depression vs. at least moderate depressive symptoms) in the general population; a statistically significant relationship was observed for pollakiuria ( $p = 0.005$ ) and for urgent pressure ( $p = 0.039$ ).

Table 4. Severity of LUTS in IPSS

Severity of LUTS	IPSS (N. %)
None or mild	62 subjects (60.78%)
Moderate	31 (30.39%)
Substantial	9 (8.82%)

The results in ICIQ-OAB and ICIQ-OABqol scales are presented in Table 5. Higher scores, and thus greater annoyance of symptoms of

bladder hyperactivity were found in the subgroup of women.

Table 5. Scores in ICIQ-OAB and ICIQ-OABqol scales

	Females (N=59 )	Males (N=43 )
ICIQ-OAB (M, SD)	4.01±2.83	2.53±2.40
ICIQ-OABqol (M, SD)	48.74±29.18	39.18±17.70



Numerous correlations between the severity and annoyance of OAB symptoms examined using the ICIQ-OAB and ICIQ-OABqol scales and the severity of depressive symptoms examined with the QIDS-SR scale were observed. The sum of points in QIDS-SR correlated with the sum of points on the ICIQ-OABqol scale for all subjects ( $r = 0.43$ ,  $p < 0.05$ ), as well as in subgroups of women ( $r = 0.45$ ,  $p < 0.05$ ) and men ( $r = 0.42$ ,  $p < 0.05$ ). The similar correlation of the sum of points in QIDS-SR was demonstrated with the sum of points on the ICIQ-OAB scale in the whole group ( $r = 0.31$ ,  $p < 0.05$ ), and in the subgroup of women examined ( $r = 0.33$ ;  $p < 0.05$ ). However, no such correlation was found in the subgroup of the studied men. Additionally, in the group of women surveyed with the sum of points in the ICIQ-OABqol scale, the sum of points in the GHQ-30 scale was correlated ( $r = 0.28$ ,  $p < 0.05$ ). In the subgroup of the studied men, the severity of OAB symptoms examined with the ICIQ-OAB scale correlated positively with the results on the QIDS-SR sleep difficulties ( $r = 0.41$ ,  $p < 0.05$ ). In the group of women, the intensity of OAB symptoms examined using the ICIQ-OAB scale correlated with the intensity of the feeling of continuous overload ( $r = 0.33$ ,  $p < 0.05$ ), impediment of mobility and activity ( $r = 0.32$ ,  $p < 0.05$ ) and the lack of meaning in life ( $r = 0.30$ ,  $p < 0.05$ ) assessed using the GHQ-30 scale.

## DISCUSSION

This study is the first in Poland to analyze the relationship between OAB and depressive symptoms. Recently, the first Polish work assessing the prevalence of LUTS among people treated psychiatrically due to depressive disorders was published. Its results indicate a significant prevalence and severity of LUTS symptoms in patients with depression, a significant impact of urological symptoms on quality of life, as well as a positive correlation of LUTS severity with depressive symptoms [23]. In the current study, a slightly higher prevalence of OAB symptoms was observed in women than in men. This is consistent with the results of other studies conducted on the general population [2,4-6,41-42]. We also observed a strong negative effect of the

severity of symptoms of bladder hyperactivity on the mental state of the subjects. The burden of illness, deterioration of activity and mobility, the feeling of lack of sense in life described by women experiencing OAB should be understood as factors aggravating depression or which may lead to its occurrence. This has already been described in previous studies [18-19, 43]. The severity of OAB symptoms and the deterioration of quality of life associated with their existence correlated positively with the severity of depressive symptoms assessed using the QIDS-SR scale. Greater severity of depressive symptoms in patients afflicted with symptoms of bladder overactivity and bidirectionality of this relationship was postulated earlier [13-16]. This is an important, clinically relevant information that should lead to coordinated psychiatric and urological diagnosis and treatment. Discrepancies observed between the results obtained by the respondents in the scales investigating the severity of depressive symptoms (QIDS-SR and HDRS) may result from the size of the examined group and from the nature of the scale (HDRS is assessed by the researcher, and QIDS-SR is the self-assessment scale). The ICIQ-OAB and ICIQ-OABqol are also self-assessment scales which may be related to the correlation of their results with those in QIDS-SR. Perhaps patients evaluating themselves describe a greater severity of symptoms than a researcher rating them with another scale? This may lead to an underestimation of the severity of OAB symptoms by those investigating this phenomenon. The authors of a review of the OAB literature published a few years ago drew attention to the inconsistency in assessing the severity of OAB, depending on the diagnostic tools used. [44].

In recent years, works investigating the effect of OAB treatment on co-occurring depressive symptoms have been published. In a prospective study on a group of 112 women treated with mirabegron due to OAB, symptomatic improvement in OAB was positively correlated with a decrease in anxiety symptoms but no correlation was observed for depressive symptoms [45]. Another large, retrospective cohort study compared a group of 1952 women with OAB treated with antimuscarinics with a group of 9762 women with OAB who were not treated with antimuscarinics [46]. Treatment with antimuscarin-

ic drugs was associated with more frequent occurrence of depression in the group of patients with OAB, especially in younger patients. The authors concluded that the use of antimuscarinic drugs increases the risk of depression. The use of anticholinergic drugs in patients with OAB is also associated with a higher risk of falls and fractures, especially in older patients (the so-called anticholinergic burden) [47]. In the study of the relationship between the use of neuromodulation in patients with OAB with comorbid depressive and anxiety symptoms, comorbidity of depression did not reduce the efficiency of neuromodulation in patients with OAB, and the improvement in depressive symptoms correlated with a reduction in the severity of OAB symptoms and anxiety symptoms [48]. Interesting conclusions have been drawn by authors of the study investigating the relationship between the use of antidepressants and the severity of OAB symptoms [49]. In this prospective cohort study, a group of 112 men treated with antidepressants for various reasons we compared with a group of 90 healthy men who were not treated with antidepressants. The incidence and severity of OAB were significantly higher in the group of men treated with antidepressants, in particular venlafaxine. The authors of a systematic review with a meta-analysis investigating the association of depression and anxiety in OAB did not find statistically significant differences between men and women in the occurrence and severity of depressive symptoms in OAB, but the frequency and severity of anxiety symptoms in OAB were significantly higher in men than in women [50]. The above examples point to a number of factors (e.g. the applied urological and psychiatric treatment, age, sex, individual genetic differences) affecting the course of OAB, as well as depression. Therefore, it can be concluded that the relationship between OAB and depression, although undoubtedly clinically significant, is complex and has a dynamic character, depending on many factors.

## CONCLUSIONS

Symptoms of OAB among patients treated for depressive disorders have high prevalence and severity. The most annoying symptoms for all patients and also separately for men and wom-

en, were nocturia and pollakiuria. In the present study, greater severity of OAB symptoms and their greater nuisance were found in women than in men. A correlation was observed between the severity of depressive symptoms and OAB. In addition, greater severity of depressive symptoms correlated with the severity of pollakiuria and urgency. OAB is a condition negatively affecting the quality of life of patients by impeding mobility and activity, and a sense of lack of meaning in life. These are factors that can lead to the occurrence or severity of depressive symptoms. Co-morbidity of depression and OAB is of significant clinical importance, which should result in further development of interdisciplinary therapeutic methods.

This study has limitations *inter alia* due to its cross-sectional nature, the lack of a control group, the size of the studied group, and large variation in pharmacological treatment. In our study, we did not indicate correlation between the severity of OAB symptoms and depressive symptoms assessed by HDRS. The differences between the results in the groups of the studied women and men can be explained by the lower number of men.

Therefore, in order to better understand the nature of the studied relationships between OAB symptoms and depressive symptoms, further, more complex multicenter cohort and prospective studies have to be carried out.

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